Mean field analysis of Williams-Bjerknes type growth

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We investigate a class of stochastic growth models involving competition between two phases in which one of the phases has a competitive advantage. The equilibrium populations of the competing phases are calculated using a mean field analysis. Regression probabilities for the extinction of the advantaged phase are calculated in a leading order approximation. The results of the calculations are in good agreement with simulations carried out on a square lattice with periodic boundaries.

The class of models are variants of the Williams-Bjerknes model for the growth of tumours in the basal layer of an epithelium. In the limit in which only one of the phases is unstable the class of models reduces to the well known variants of the Eden model.

1 Introduction

Stochastic pattern formation is ubiquitous in science and technology (see, e.g., [1–4] and the many references therein). Some examples include viscous fingering in fluids, dendritic crystallization, electro-deposition, dielectric breakdown and the growth of bacterial colonies. It is remarkable that, despite their disparate physical origins, many such patterns can essentially be described by one of two generic models. These models are distinguished by the nature of the stochastic growth at the interface, which is usually taken to be either: (i) uniform – as in the Eden model [5,6], or (ii) Laplacian – as in the diffusion-limited aggregation model [7].

These generic models and their numerous refinements have been intensively studied and have proved highly successful in describing the growth of patterns

in which one stable phase propagates into a second unstable phase. For example, in the formation of snowflakes the snow crystal (stable phase) propagates into water vapour (unstable phase). In viscous fingering a low viscosity fluid (stable phase) is pumped under pressure into a background high viscosity fluid (unstable phase). These are examples of Laplacian growth processes. An example of a uniform growth process is the spread of a bacterial colony (stable phase) via cell-division into a nutrient-rich environment (unstable phase) [8].

However, many important growth processes have two or more competing unstable phases. An example is the Williams-Bjerknes (WB) model [9] for the growth of tumours, in which both the cancerous cells and the normal cells are unstable (both may be displaced by cell division). The limiting growth is governed by this competition. The cancerous cells have the competitive advantage of dividing faster than normal cells. Importantly, early simulations of the model [9] revealed that the invasive nature of the tumours can be accounted for solely by an almost evenly balanced contest between the cancerous cells and the normal cells. These early simulations also investigated the regression probability, defined as the probability that the advantaged phase, starting out as a single seed, will become extinct under the growth process. Subsequent simulations [10] and rigorous mathematical studies [11,12] revealed that the abnormal region, whenever it survives, can be described as an asymptotic shape (with a one-dimensional boundary), the average radius of which grows linearly in time.

In this paper we introduce a class of uniform stochastic growth models (which includes the WB model) involving competition between two phases. The equilibrium populations of the competing phases are calculated using a mean field analysis similar to that used recently for a dynamical model of virus spread [13]. Leading order approximations for regression probabilities are also calculated.

The mean field results and regression results are in good agreement with simulations carried out on a square lattice with periodic boundaries.

2   Competing Growth Models - Mean-Field Equations

Consider a regular lattice with N sites where N_A are of type A and N_B are type B. Define an interface site as one which has one or more nearest neighbouring sites of the opposite type. Let $\mathcal{N}_A$ and $\mathcal{N}_B$ denote the number of type A interface sites and type B interface sites respectively. The total number of nearest neighbour sites surrounding a lattice site is the lattice co-ordination number denoted here by n_c (for example, $n_c = 4$ on the square lattice).

In the models below the numbers of type A sites and type B sites change in time as a consequence of interface interactions which occur when an interface site is changed into the opposite type. Let $p_{i \to B}$ denote the probability for site i to be changed to a type B site and similarly for $p_{i \to A}$. The complete set of transition probabilities for the site i are then;

$$p_{i(B) \to A} = p_{i \to A} \delta_{i,B}, \tag{1}$$
$$p_{i(A) \to B} = p_{i \to B} \delta_{i,A}, \tag{2}$$
$$p_{i(A) \to A} = p_{i \to A} \delta_{i,A}, \tag{3}$$
$$p_{i(B) \to B} = p_{i \to B} \delta_{i,B}. \tag{4}$$

where $i(A)$ and $i(B)$ is used to represent the situation in which site i is a type A site and a type B site respectively. The mean field probability that a B site will be changed into an A site is thus

$$p_{B \to A} = \sum_i^N p_{i \to A} \delta_{i,B}. \tag{5}$$

Similarly

$$p_{A \to B} = \sum_i^N p_{i \to B} \delta_{i,A} \tag{6}$$

is the mean field probability that an A site will be changed into a B site. Using these probabilities we can write down general mean field population equations for this class of models which relates the numbers of species before (time t) and after (time $t + 1$) an interface interaction:

$$N_A(t + 1) = p_{B \to A}(t) - p_{A \to B}(t) + N_A(t), \tag{7}$$
$$N_B(t + 1) = p_{A \to B}(t) - p_{B \to A}(t) + N_B(t). \tag{8}$$

The mean field steady state defined by $N_A(t + 1) = N_A(t) = N_A^*$ and $N_B(t + 1) = N_B(t) = N_B^*$ thus yields the (equivalent) equilibrium conditions

$$p_{B \to A}^* = p_{A \to B}^*, \tag{9}$$
$$\sum_i^N p_{i \to A}^* \delta_{i,B} = \sum_i^N p_{i \to B}^* \delta_{i,A}. \tag{10}$$

We shall make use of both forms of the mean-field equilibrium condition in the following. Note that the steady state mean field probabilities $p_{B \to A}^*$ and $p_{A \to B}^*$ are in general functions of $N_A^*, \mathcal{N}_A^*, N_B^*, \mathcal{N}_B^*$.

3   Williams-Bjerknes Model

In the WB model, the spread of cancers is modelled by the growth of two types of cells, cancerous cells and normal cells, which compete via cell division in a basal layer. The cancerous cells are taken to divide κ times faster than normal cells. This factor κ is called the carcinogenic advantage. It is supposed that when a cell in the basal layer divides the daughter cell displaces a neighbouring cell up out of the basal layer [14]. The implementation of the model is straightforward. Start with a regular lattice of sites (basal layer) labelled type A (cancerous) or type B (normal). Select a site at random with a bias (due to the carcinogenic advantage) for selecting type A. Choose one of the neighbouring sites of the selected site at random and convert it to the same type as the selected site. Typically there are many growth steps that do not change the configuration of the basal layer.

We have simulated this model within a rectangular region covering $[0, 100] \times [-100, 100]$ square lattice sites using periodic boundaries in both directions. Initially the top half of the rectangular region is comprised of abnormal cells and the bottom half is comprised of the normal cells. The configurations of normal and abnormal cells for the case $\kappa = 2$ are shown at four different time snapshots in Fig. 1. Two points of note are: i) the interface between normal and abnormal cells is highly irregular; ii) the ratio abnormal cells to normal cells increases in time until (on average) the advantaged species completely dominates.

3.1   Mean Field Equilibrium

To determine the mean field equilibrium state for this model we first define the model transition probabilities. The probability that a site i will be changed $(B \to A)$ or reconfigured $(A \to A)$ into type A is

$$p_{i \to A} = \left(\frac{\kappa N_A}{\kappa N_A + N_B} \right) \left(\frac{n_i(A)}{N_A} \right) \left(\frac{1}{n_c} \right), \tag{11}$$

where $n_i(A)$ is the number of neighbouring A sites adjoining site i. The first factor is the carcinogenic advantage for a division of an A cell. The second factor is the probability that the A cell chosen for division is one of the neighbours of site i. The final factor is the probability that if a neighbouring A cell for site i is chosen for division it will displace the cell at site i out of the basal layer leaving an A cell at that location. Similarly the probability that a site i

4

will be changed or reconfigured into type B is

$$p_{i \to B} = \left(\frac{N_B}{\kappa N_A + N_B} \right) \left(\frac{n_i(B)}{N_B} \right) \left(\frac{1}{n_c} \right). \tag{12}$$

The normalization of the probabilities,

$$P = \sum_i^N (p_{i \to A} + p_{i \to B}) = 1, \tag{13}$$

follows immediately from the identities

$$\sum_i^N \frac{n_i(A)}{n_c} = N_A, \tag{14}$$

$$\sum_i^N \frac{n_i(B)}{n_c} = N_B. \tag{15}$$

Substituting the expressions for the transition probabilities (11), (12) into the mean field equilibrium condition (10) yields

$$\kappa \sum_i^N n_i(A)\delta_{i,B} = \sum_i^N n_i(B)\delta_{i,A}. \tag{16}$$

This result can be simplified by the identity

$$\sum_i^N n_i(A)\delta_{i,B} = \sum_i^N n_i(B)\delta_{i,A}; \tag{17}$$

which follows from the Eqs (14), (15), together with the neighbour summation rule $n_i(A) + n_i(B) = n_c$. Using the identity (17) the mean field equilibrium result (16) simplifies to

$$\kappa = 1. \tag{18}$$

From our stochastic simulations described above we have have obtained a plot in Fig. 2 of the time taken for all B cells to die out ($\kappa > 1$) and the time for all A cells to die out ($\kappa < 1$) as a function of $\log \kappa$. The extinction time rapidly increases with decreasing $|\kappa - 1|$ and there is a clear possibility for a steady state with both species at $\kappa = 1$.

A different form of the equilibrium condition can be derived by writing the mean field probability that any B type cell is changed into an A type cell as

$$p_{B \to A} = \left(\frac{\kappa N_A}{\kappa N_A + N_B} \right) \left(\frac{\mathcal{N}_A}{N_A} \right) \alpha_{B \to A}. \tag{19}$$

The first factor on the right is the probability that an A cell divides, the second factor is the probability that the dividing A cell is an interface cell and the third factor is the probability that A interface cells displace B interface cells (there is a finite probability that A cells might divide without any resultant change in the configuration). Similarly the mean field probability that any A type cell is changed into a B type cell can be written as

$$p_{A \to B} = \left(\frac{N_B}{\kappa N_A + N_B} \right) \left(\frac{\mathcal{N}_B}{N_B} \right) \alpha_{A \to B}. \tag{20}$$

Substituting (19) and (20) into the mean field equilibrium condition (9) now yields

$$\kappa \mathcal{N}_A \alpha_{B \to A} = \mathcal{N}_B \alpha_{A \to B}. \tag{21}$$

Comparing (21) with the previous equilibrium condition (18) we obtain the additional equilibrium result

$$\frac{\alpha_{A \to B}}{\alpha_{B \to A}} = \frac{\mathcal{N}_A}{\mathcal{N}_B}. \tag{22}$$

Note that in general we can write

$$\sum_i^N n_i(B) \delta_{i,A} = \alpha_B \mathcal{N}_B, \tag{23}$$

where the factor α_B is included because some of the B interface cells are counted more than once in the sum, and similarly

$$\sum_i^N n_i(A) \delta_{i,B} = \alpha_A \mathcal{N}_A. \tag{24}$$

Combining (23) and (24) with the identity (17) thus yields

$$\alpha_A \mathcal{N}_A = \alpha_B \mathcal{N}_B. \tag{25}$$

6

Comparing the general result (25) with the equilibrium condition (22) we now have

$$\frac{\alpha_A}{\alpha_B} = \frac{\alpha_{B \to A}}{\alpha_{A \to B}}. \tag{26}$$

3.2 Regression

Here we consider the case in which a single cancerous site ($N_A = 1$) is surrounded by normal sites ($N_B = N - 1$). The transition probabilities are thus

$$p_{i(B) \to A} = \left(\frac{\kappa}{\kappa + N - 1} \right) n_i(A) \frac{1}{n_c} \delta_{i,B}, \tag{27}$$

$$p_{i(A) \to B} = \left(\frac{N - 1}{\kappa + N - 1} \right) \left(\frac{n_i(B)}{N - 1} \right) \frac{1}{n_c} \delta_{i,A}, \tag{28}$$

$$p_{i(A) \to A} = \left(\frac{\kappa}{\kappa + N - 1} \right) n_i(A) \frac{1}{n_c} \delta_{i,A}, \tag{29}$$

$$p_{i(B) \to B} = \left(\frac{N - 1}{\kappa + N - 1} \right) \left(\frac{n_i(B)}{N - 1} \right) \frac{1}{n_c} \delta_{i,B}. \tag{30}$$

Summing over the lattice sites we have

$$p_{B \to A} = \left(\frac{\kappa}{\kappa + N - 1} \right), \tag{31}$$

$$p_{A \to B} = \left(\frac{1}{\kappa + N - 1} \right), \tag{32}$$

$$p_{A \to A} = 0, \tag{33}$$

$$p_{B \to B} = \left(\frac{N - 2}{\kappa + N - 1} \right). \tag{34}$$

The probability $p_{A \to B}$ is the probability for regression in one step. The probability for regression without any growth within m steps is given by

$$p_{A \to B}(m) = \sum_{k=1}^{m} (p_{B \to B})^{k-1} p_{A \to B}, \tag{35}$$

$$= \frac{1 - \left(\frac{N-2}{\kappa+N-1} \right)^m}{\kappa + 1}, \tag{36}$$

and the probability for regression without growth after infinitely many steps is

$$p_{A \to B}(\infty) = \sum_{k=1}^{\infty} (p_{B \to B})^{k-1} p_{A \to B}, \qquad (37)$$

$$= \frac{1}{\kappa + 1}. \qquad (38)$$

We anticipate that the probability for regression without growth will be the dominant term in the overall probability for regression, which includes the probability for regression after growth, so that (38) may be taken as a leading order approximation. To investigate this further consider regression within three steps. The possible scenarios and associated probabilities are:

$$A \to B \,;\, B \to B \,;\, B \to B : \qquad p_{A \to B}; \qquad (39)$$
$$B \to B \,;\, A \to B \,;\, B \to B : \qquad p_{B \to B} p_{A \to B}; \qquad (40)$$
$$B \to B \,;\, B \to B \,;\, A \to B : \qquad (p_{B \to B})^2 p_{A \to B}; \qquad (41)$$
$$B \to A \,;\, A \to B \,;\, A \to B : \qquad p_{B \to A} \hat{p}_{A \to B} p_{A \to B}; \qquad (42)$$

The sum of the probabilities in the first three scenarios above is the probability for regression without growth within three steps (Eq (35) with $m = 3$) and

$$\hat{p}_{A \to B} = \left(\frac{3}{2}\right) \left(\frac{N-2}{2\kappa + N - 2}\right) \left(\frac{1}{N-2}\right) \qquad (43)$$

is the probability $A \to B$ in a cluster with two adjacent type A cells. It immediately follows that the ratio the probability for regression after growth within three steps to the probability for regression without growth within three steps scales as $1/N^3$.

We have studied regression in simulations with $\kappa = 2$ over $[-10, 10] \times [-10, 10]$ sites on a square lattice. In Fig. 3 we have plotted the frequency of regression within three, five and ten steps versus the total number of runs used in the frequency estimate, over a range of the total number of runs up to 10^6. The upper two horizontal lines on the plot are the probabilites for regression without growth after five and ten steps and the lower horizontal line is the full probability for regression after three steps. The comparison between the Monte Carlo results and the algebraic regression results provides evidence that regression without growth dominates the regression process.

3.3 Limit $\kappa \to \infty$

In the limit $\kappa \to \infty$ the B cells never divide and the transition probabilities become:

$$p_{i(A)\to B} = 0, \tag{44}$$

$$p_{i(B)\to B} = 0, \tag{45}$$

$$p_{i(A)\to A} = \left(\frac{n_i(A)}{N_A}\right)\frac{1}{n_c}\delta_{i,A}, \tag{46}$$

$$p_{i(B)\to A} = \left(\frac{n_i(A)}{N_A}\right)\frac{1}{n_c}\delta_{i,B}. \tag{47}$$

In this case there are only two possible events $A \to A$ and $B \to A$. The event $A \to A$ affects the time scale for configurational changes but does not affect the configurations themselves. Hence if we do not concern ourselves with the time scales for change we can set $p_{i(A)\to A} = 0$ and renormalize

$$p_{i(B)\to A} = \frac{n_i(A)\delta_{i,A}}{\sum_i^{\mathcal{N}_B} n_i(A)} \tag{48}$$

where the sum is over all type B interface sites. In this limit the model is equivalent to the original model introduced by Eden [5,6], which is also referred to as the Eden B model [15].

4   Interface Model

In this model only interface sites are considered for division. Select an interface site at random with a bias for selecting type A and convert one of the neighbouring sites of the selected site to a site of the same type. Note that this model still allows non-configurational changes where the number of type A interface sites and the number of type B interface sites may both be conserved after a growth event. Let $\bar{n}_i(A)$ denote the number of type A interface sites adjoining site i and let $\bar{n}_i(B)$ denote the number of type B interface sites adjoining site i. The transition probabilities for site i to change to an A site or a B site are

$$p_{i\to A} = \frac{\kappa\mathcal{N}_A}{\kappa\mathcal{N}_A + \mathcal{N}_B}\frac{\bar{n}_i(A)}{\mathcal{N}_A}\frac{1}{n_c}, \tag{49}$$

$$p_{i\to B} = \frac{\mathcal{N}_B}{\kappa\mathcal{N}_A + \mathcal{N}_B}\frac{\bar{n}_i(B)}{\mathcal{N}_B}\frac{1}{n_c}. \tag{50}$$

9

4.1 Mean Field Equilibrium

Substituting (49,50) into the equilibrium condition (10) yields

$$\kappa \sum_i^N \bar{n}_i(A)\delta_{i,B} = \sum_i^N \bar{n}_i(B)\delta_{i,A}. \tag{51}$$

We can simplify this expression by noting that all type A sites adjoining a type B site are interface sites and vice-versa hence we have the identities

$$\sum_i^N \bar{n}_i(A)\delta_{i,B} = \sum_i^N n_i(A)\delta_{i,B}, \tag{52}$$

$$\sum_i^N \bar{n}_i(B)\delta_{i,A} = \sum_i^N n_i(B)\delta_{i,A}. \tag{53}$$

Substituting the above identities together with the identity (17) we obtain the equilibrium condition

$$\kappa = 1. \tag{54}$$

For other values of κ it is expected that the system will evolve until all sites are the same type; type A for $\kappa > 1$ and type B for $\kappa < 1$.

The mean field equilibrium results have been found to provide a good description of the long time populations in stochastic simulations of this model carried out on $[0, 100] \times [-100, 100]$ square lattice sites with the top half of the region initially comprised of abnormal cells and the bottom half initially comprised of normal cells. In Fig. 4 we show four different time snapshots for the case $\kappa = 2$.

As in the WB model the interface is highly irregular and the advantaged species completely dominates. However, the time taken for the extinction of the disadvantaged species is considerably less than for the WB model. The extinction times for the interface model over a range of κ are shown in Fig. 5. As in the original WB model the extinction time rapidly increases with decreasing $|\kappa - 1|$ and there is again a clear possibility for a steady state with both species at $\kappa = 1$. Comparing Fig. 2 and Fig. 5 we see that for $\approx 10^4$ cells the extinction time is an order of magnitude less in the interface model than in the WB model.

4.2 Regression

In the case where initially we have a single type A site surrounded by type B sites the transition probabilities are

$$p_{B \to A} = \frac{\kappa}{\kappa + 4}, \tag{55}$$

$$p_{A \to B} = \frac{1}{\kappa + 4}, \tag{56}$$

$$p_{A \to A} = 0, \tag{57}$$

$$p_{B \to B} = \frac{3}{\kappa + 4}. \tag{58}$$

The probability for regression without growth after m steps is

$$p_{A \to B}(m) = \sum_{k=1}^{m} \left(\frac{3}{\kappa + 4} \right)^{k-1} \frac{1}{(\kappa + 4)}, \tag{59}$$

$$= \frac{1 - \left(\frac{3}{\kappa + 4} \right)^{m}}{\kappa + 1}. \tag{60}$$

The probability for regression without growth after infinitely many steps is again

$$p_{A \to B}(\infty) = \frac{1}{\kappa + 1}. \tag{61}$$

4.3 Limit $\kappa \to \infty$

The $\kappa \to \infty$ limit of this interface model is equivalent to the $\kappa \to \infty$ limit of the WB model and is thus equivalent to the Eden B model.

5 Selective Interface Model

In the selective interface model an interface site is selected at random with a bias for selecting a type A site. Then one of the *interface* neighbouring sites of the selected site is chosen at random and converted to the same type as the initially selected site. The transition probabilities are

$$p_{i \to A} = \frac{\kappa \mathcal{N}_A}{\kappa \mathcal{N}_A + \mathcal{N}_B} \frac{1}{\mathcal{N}_A} \sum_{i'}^{n_c} \frac{\delta_{i',A}}{n_{i'}(B)}, \tag{62}$$

11

$$p_{i \to B} = \frac{\mathcal{N}_B}{\kappa \mathcal{N}_A + \mathcal{N}_B} \frac{1}{\kappa + 1} \frac{1}{\mathcal{N}_B} \sum_{i'}^{n_c} \frac{\delta_{i',B}}{n_{i'}(A)}, \tag{63}$$

where the sum $\sum_{i'}^{n_c}$ denotes a sum over the neighbours of site i.

5.1   Mean Field Equilibrium

The mean field equilibrium condition (10) for this model is

$$\kappa \sum_i \sum_{i'}^{n_c} \frac{\delta_{i',A}}{n_{i'}(B)} \delta_{i,B} = \sum_i \sum_{i'}^{n_c} \frac{\delta_{i',B}}{n_{i'}(A)} \delta_{i,A}. \tag{64}$$

This expression can be simplified. First we reverse the order of the sum over interface sites, $\sum_i$, and the sum over neighbours, $\sum_i'$, to obtain

$$\kappa \sum_i \sum_{i'}^{n_c} \delta_{i',B} \frac{\delta_{i,A}}{n_i(B)} = \sum_i \sum_{i'}^{n_c} \delta_{i',A} \frac{\delta_{i,B}}{n_i(A)}. \tag{65}$$

It is now a trivial matter to perform the sum over neighbours;

$$\sum_{i'}^{n_c} \delta_{i',B} = n_i(B), \tag{66}$$

$$\sum_{i'}^{n_c} \delta_{i',A} = n_i(A), \tag{67}$$

leading to the equilibrium condition

$$\kappa \mathcal{N}_A = \mathcal{N}_B. \tag{68}$$

In general we might expect that the number of type A interface sites and the number of type B interface sites are approximately equal. The mean field steady state equilibrium that is consistent with this expectation is; $\kappa = 1$ and $\mathcal{N}_B = \mathcal{N}_A$, or $\mathcal{N}_B = \mathcal{N}_A = 0$. The result $\mathcal{N}_B = \mathcal{N}_A = 0$ is consistent with all type A sites for $\kappa > 1$ and all type B sites for $\kappa < 1$.

5.2   Regression

In the case where a single type A site is surrounded by n_c type B sites the transition probabilities reduce to

$$p_{B \to A} = \frac{\kappa}{\kappa + 4}, \tag{69}$$

$$p_{A \to B} = \frac{4}{\kappa + 4}, \tag{70}$$

so that the probability for regression without growth in this model is $\frac{4}{\kappa+4}$.

5.3 Limit $\kappa \to \infty$

In the limit $\kappa \to \infty$ the transition probability is

$$p_{i \to A} = \frac{1}{\mathcal{N}_A} \sum_{i'}^{n_c} \frac{\delta_{i',A}}{n_{i'}(B)}, \tag{71}$$

which is equivalent to the Eden C model [15].

6 Cross-Feeding Model

Consider a colony of $\mathcal{N}_A$ type A interface cells and $\mathcal{N}_B$ type B interface cells. Select a cell at random with a bias for choosing type B. Convert the chosen cell to the opposite type. The transition probabilities are

$$p_{i(B) \to A} = \frac{\kappa \mathcal{N}_A}{\kappa \mathcal{N}_A + \mathcal{N}_B} \frac{1}{\mathcal{N}_B} \delta_{i,B}, \tag{72}$$

$$p_{i(A) \to B} = \frac{\mathcal{N}_B}{\kappa \mathcal{N}_A + \mathcal{N}_B} \frac{1}{\mathcal{N}_A} \delta_{i,A}. \tag{73}$$

Hence

$$p_{B \to A} = \frac{\kappa \mathcal{N}_A}{\kappa \mathcal{N}_A + \mathcal{N}_B}, \tag{74}$$

$$p_{A \to B} = \frac{\mathcal{N}_B}{\kappa \mathcal{N}_A + \mathcal{N}_B}, \tag{75}$$

so that the probability for regression without growth is $\frac{\mathcal{N}_B}{\kappa \mathcal{N}_A + \mathcal{N}_B}$ and the equilibrium condition is $\kappa \mathcal{N}_A = \mathcal{N}_B$.

In the $\kappa \to \infty$ limit the probability for a particular B cell to become an A cell is $1/\mathcal{N}_B$ which is equivalent to the Eden A model [15].

7 Cross-Feeding Model with Neighbour Bias

Consider a colony of $\mathcal{N}_A$ type A interface cells and $\mathcal{N}_B$ type B interface cells. Select either the set of A cells or the set of B cells with a bias for choosing the set of B cells. Pick a cell at random from the selected set with a weighting according to the number of neighbouring cells of opposite type. Convert the chosen cell to the opposite type. The transition probabilities are

$$p_{i(B)\to A} = \frac{\kappa \mathcal{N}_A}{\kappa \mathcal{N}_A + \mathcal{N}_B} \frac{n_i(A)}{\mathcal{N}_B} \delta_{i,\bar{B}}, \tag{76}$$

$$p_{i(A)\to B} = \frac{\mathcal{N}_B}{\kappa \mathcal{N}_A + \mathcal{N}_B} \frac{n_i(B)}{\mathcal{N}_A} \delta_{i,\bar{A}}, \tag{77}$$

where the $\bar{B}$ denotes an interface B site and the $\bar{A}$ denotes an interface A site. In this model the transition probabilities are not automatically normalized. However, it is a simple matter to calculate the normalization

$$S = \frac{1}{\kappa \mathcal{N}_A + \mathcal{N}_B} \left(\frac{\kappa \mathcal{N}_A}{\mathcal{N}_B} + \frac{\mathcal{N}_B}{\mathcal{N}_A} \right) \sum_i^N n_i(A)\delta_{i,\bar{B}}, \tag{78}$$

$$= \frac{1}{\kappa \mathcal{N}_A + \mathcal{N}_B} \left(\frac{\kappa \mathcal{N}_A}{\mathcal{N}_B} + \frac{\mathcal{N}_B}{\mathcal{N}_A} \right) \sum_i^N n_i(B)\delta_{i,\bar{A}}, \tag{79}$$

where we have used the identity

$$\sum_i^N n_i(A)\delta_{i,\bar{B}} = \sum_i^N n_i(B)\delta_{i,\bar{A}}, \tag{80}$$

which follows immediately from the identity (17).

Summing over all sites we obtain the mean field probability that a B cell becomes an A cell and vice-versa:

$$p_{B\to A} = \frac{\kappa \frac{\mathcal{N}_A}{\mathcal{N}_B}}{\kappa \frac{\mathcal{N}_A}{\mathcal{N}_B} + \frac{\mathcal{N}_B}{\mathcal{N}_A}}, \tag{81}$$

$$p_{A\to B} = \frac{\frac{\mathcal{N}_B}{\mathcal{N}_A}}{\kappa \frac{\mathcal{N}_A}{\mathcal{N}_B} + \frac{\mathcal{N}_B}{\mathcal{N}_A}}, \tag{82}$$

$$\tag{83}$$

The mean field equilibrium condition in this model is thus $\kappa \mathcal{N}_A{}^2 = \mathcal{N}_B{}^2$. Again if we use the approximation $\mathcal{N}_A \approx \mathcal{N}_B$ then the equilibrium condition

is satisfied by; either $\kappa = 1$ and $\mathcal{N}_A \approx \mathcal{N}_B$, or $\mathcal{N}_A = \mathcal{N}_B = 0$. The latter case occurring when one or other species completely dominates.

In this model if we start with a single type A cell surrounded by n_c type B cells it is a simple matter to show that the probability for regression without growth is $\frac{4}{\kappa+4}$.

The $\kappa \to \infty$ limit of this model reduces to the original Eden model [5,6], as in (48) above.

8 Discussion

In this paper we have introduced a class of stochastic growth models involving competition between two phases in which one of the phases has a competitive advantage κ. This class of models includes the WB model for tumour growth. In the limit $\kappa \to \infty$ where only one of the phases is unstable the class of models reduces to well known variants of the Eden model. We have derived mean field equilibrium results and regression probabilities (expressing the probability that the advantaged phase dies out) for the class of competitive growth models. The results are found to be in good agreement with stochastic simulations carried out on a square lattice with periodic boundaries.

In the class of models studied here an equilibrium configuration with both types of cells can only occur when $\kappa = 1$. An oft quoted result for the WB model is that the regression probability is $\frac{1}{\kappa}$ (or $\frac{1}{\kappa+1}$). Our simulations and analysis show that the result $\frac{1}{\kappa+1}$ applies both to interface implementations of the WB model and to the full WB model.

In subsequent work we plan to explore the important question of the rate of approach to the equilibrium state.

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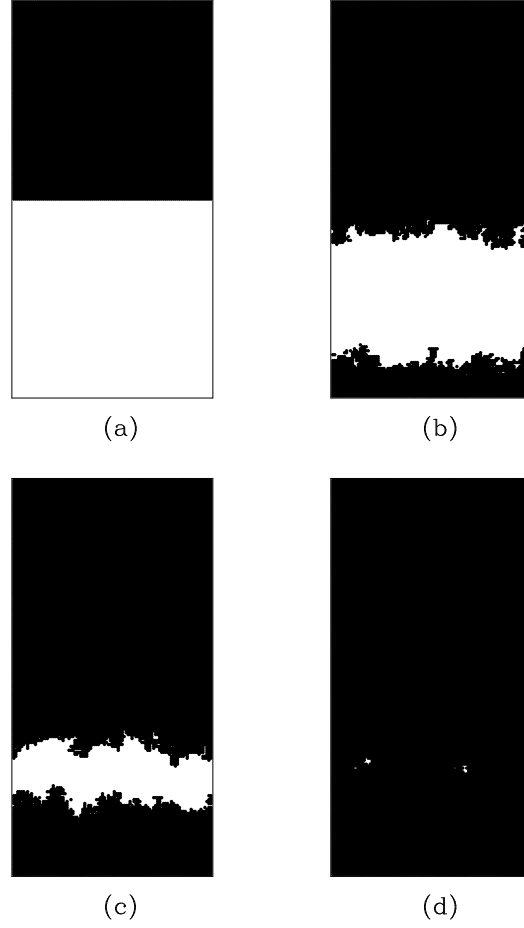[15] R. Jullien and R. Botet, J. Phys. A 18 (1985) 2279.

Fig. 1. Configurations of normal cells (white) and abnormal cells (black) in the WB model with carcinogenic advantage $\kappa = 2$; (a) initially, (b) after 8×10^5 steps, (c) after 16×10^5 steps, (d) after 24×10^5 steps.

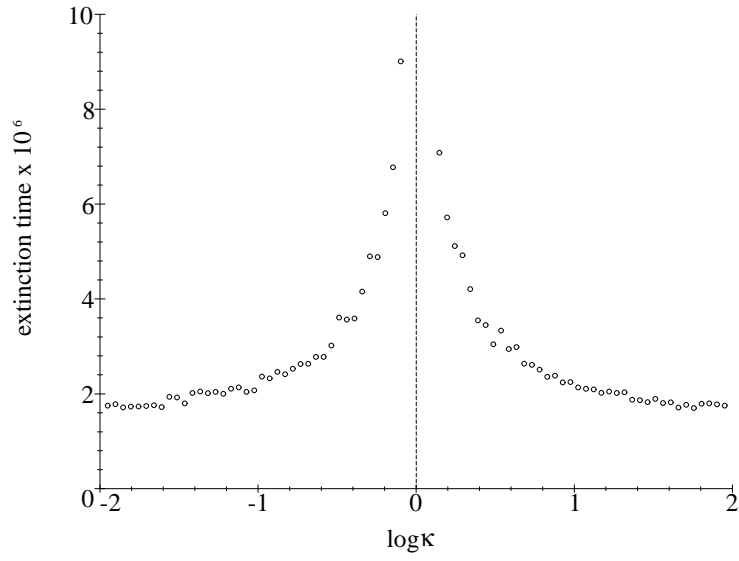Fig. 2. Time taken for the extinction of normal cells ($\kappa > 1$) and the extinction of abnormal cells ($\kappa < 1$) as a function of $\log \kappa$ in the WB model.
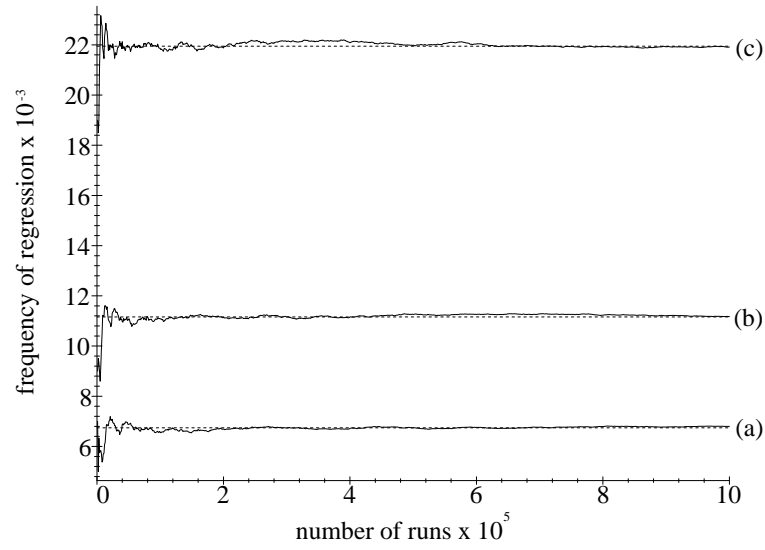
Fig. 3. The frequency of regression within (a) three (b) five and (c) ten steps versus the total number of runs used in the frequency estimate for the WB model. The lower horizontal line is the probability of regression after three steps and the two upper horizontal lines are the probabilities for regression without growth after (b) five and (c) ten steps.
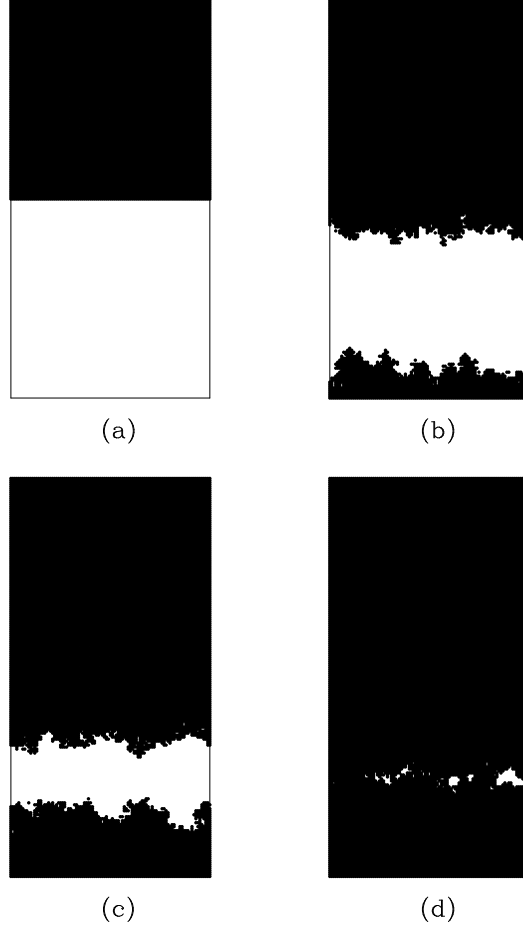
Fig. 4. Configurations of normal cells (white) and abnormal cells (black) in the Interface Model model with carcinogenic advantage $\kappa = 2$; (a) initially, (b) after 25×10^3 steps, (c) after 50×10^3 steps, (d) after 75×10^3 steps.
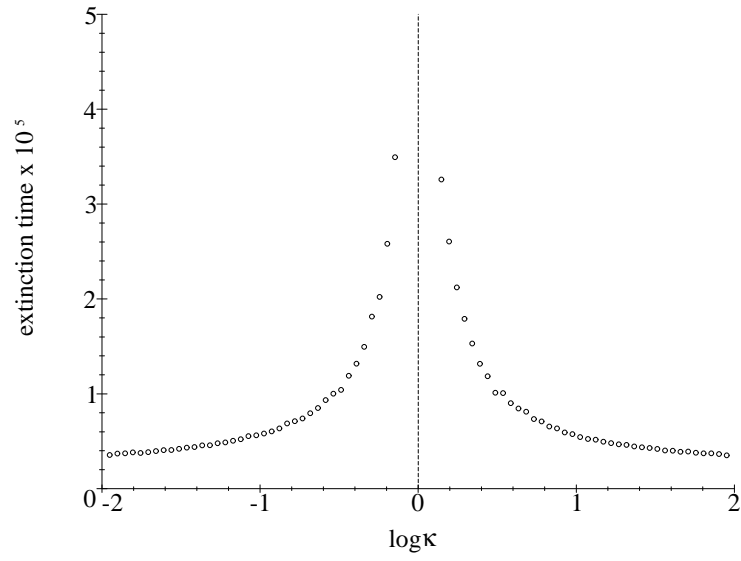
Fig. 5. Time taken for the extinction of normal cells ($\kappa > 1$) and the extinction of abnormal cells ($\kappa < 1$) as a function of $\log \kappa$ in the Interface Model.